General

Guideline Title

Clinical policy: critical issues in the evaluation and management of adult patients presenting to the emergency department with seizures.

Bibliographic Source(s)

Huff JS, Melnick ER, Tomaszewski CA, Thiessen ME, Jagoda AS, Fesmire FM, American College of Emergency Physicians. Clinical policy: critical issues in the evaluation and management of adult patients presenting to the emergencyÂ department with seizures. Ann Emerg Med. 2014 Apr;63(4):437-447.e15. [55 references] PubMed

Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: Clinical policy: critical issues in the evaluation and management of adult patients presenting to the emergency department with seizures. Ann Emerg Med. 2004 May;43(5):605-25. [95 references]

Regulatory Alert

FDA Warning/Regulatory Alert

Note from the National Guideline Clearinghouse: This guideline references a drug(s) for which important revised regulatory and/or warning information has been released.

- December 14, 2016 – General anesthetic and sedation drugs : The U.S. Food and Drug Administration (FDA) is warning that repeated or lengthy use of general anesthetic and sedation drugs during surgeries or procedures in children younger than 3 years or in pregnant women during their third trimester may affect the development of children's brains. Consistent with animal studies, recent human studies suggest that a single, relatively short exposure to general anesthetic and sedation drugs in infants or toddlers is unlikely to have negative effects on behavior or learning. However, further research is needed to fully characterize how early life anesthetic exposure affects children's brain development.

Recommendations

Major Recommendations

Definitions for the strength of evidence (Class I-III) and strength of recommendations (Level A-C) are provided at the end of the "Major Recommendations" field.

1. In patients with a first generalized convulsive seizure who have returned to their baseline clinical status, should antiepileptic therapy be initiated in the emergency department (ED) to prevent additional seizures?
   Patient Management Recommendations

   Level A recommendations. None specified.

   Level B recommendations. None specified.

   Level C recommendations.

   1. Emergency physicians need not initiate antiepileptic medication* in the ED for patients who have had a first *provoked* seizure. Precipitating medical conditions should be identified and treated.
   2. Emergency physicians need not initiate antiepileptic medication* in the ED for patients who have had a first *unprovoked* seizure without evidence of brain disease or injury.
   3. Emergency physicians may initiate antiepileptic medication* in the ED, or defer in coordination with other providers, for patients who experienced a first *unprovoked* seizure with a remote history of brain disease or injury.

   *Antiepileptic medication in this document refers to medications prescribed for seizure prevention.

2. In patients with a first unprovoked seizure who have returned to their baseline clinical status in the ED, should the patient be admitted to the hospital to prevent adverse events?
   Patient Management Recommendations

   Level A recommendations. None specified.

   Level B recommendations. None specified.

   Level C recommendations. Emergency physicians need not admit patients with a first unprovoked seizure who have returned to their clinical baseline in the ED.

3. In patients with a known seizure disorder in which resuming their antiepileptic medication in the ED is deemed appropriate, does the route of administration impact recurrence of seizures?
   Patient Management Recommendations

   Level A recommendations. None specified.

   Level B recommendations. None specified.

   Level C recommendations. When resuming antiepileptic medication in the ED is deemed appropriate, the emergency physician may administer intravenous (IV) or oral medication at their discretion.

4. In ED patients with generalized convulsive status epilepticus who continue to have seizures despite receiving optimal dosing of a benzodiazepine, which agent or agents should be administered next to terminate seizures?
   Patient Management Recommendations

   Level A recommendations. Emergency physicians should administer an additional antiepileptic medication in ED patients with refractory status epilepticus who have failed treatment with benzodiazepines.

   Level B recommendations. Emergency physicians may administer IV phenytoin, fosphenytoin, or valproate in ED patients with refractory status epilepticus who have failed treatment with benzodiazepines.

   Level C recommendations. Emergency physicians may administer IV levetiracetam, propofol, or barbiturates in ED patients with refractory status epilepticus who have failed treatment with benzodiazepines.

Definitions:

Strength of Evidence

Literature Classification Schema*

Design/Class	Therapy†	Diagnosis‡	Prognosis§
1	Randomized, controlled trial or	Prospective cohort using a criterion standard	Population prospective cohort or

Design/Class	Therapy†	Diagnosis‡	Prognosis§
	meta-analysis of randomized trials	or meta-analysis of prospective studies	meta-analysis of prospective studies
2	Nonrandomized trial	Retrospective observational	Retrospective cohort Case control
3	Case series Case report Other (e.g., consensus, review)	Case series Case report Other (e.g., consensus, review)	Case series Case report Other (e.g., consensus, review)

*Some designs (e.g., surveys) will not fit this schema and should be assessed individually.

†Objective is to measure therapeutic efficacy comparing interventions.

‡Objective is to determine the sensitivity and specificity of diagnostic tests.

§Objective is to predict outcome including mortality and morbidity.

Approach to Downgrading Strength of Evidence*

	Design/Class		
Downgrading	**1**	**2**	**3**
None	I	II	III
1 level	II	III	X
2 levels	III	X	X
Fatally flawed	X	X	X

*See the "Description of Methods Used to Analyze the Evidence" field for more information.

Strength of recommendations regarding each critical question were made by subcommittee members using results from strength of evidence grading, expert opinion, and consensus among subcommittee members according to the following guidelines:

Strength of Recommendations

Level A recommendations. Generally accepted principles for patient care that reflect a high degree of clinical certainty (i.e., based on evidence from 1 or more Class of Evidence I or multiple Class of Evidence II studies).

Level B recommendations. Recommendations for patient care that may identify a particular strategy or range of strategies that reflect moderate clinical certainty (i.e., based on evidence from 1 or more Class of Evidence II studies or strong consensus of Class of Evidence III studies).

Level C recommendations. Recommendations for patient care that are based on evidence from Class of Evidence III studies or, in the absence of any adequate published literature, based on expert consensus. In instances where consensus recommendations are made, "consensus" is placed in parentheses at the end of the recommendation.

There are certain circumstances in which the recommendations stemming from a body of evidence should not be rated as highly as the individual studies on which they are based. Factors such as heterogeneity of results, uncertainty about effect magnitude and consequences, and publication bias, among others, might lead to such a downgrading of recommendations.

Clinical Algorithm(s)

None provided

Scope

Disease/Condition(s)

Seizures

- Provoked seizure (acute symptomatic seizure)
- Unprovoked seizure (including remote symptomatic seizure)

Guideline Category

Evaluation

Management

Prevention

Treatment

Clinical Specialty

Emergency Medicine

Internal Medicine

Neurology

Intended Users

Physicians

Guideline Objective(s)

To derive evidence-based recommendations to help clinicians answer the following critical questions:

- In patients with a first generalized convulsive seizure who have returned to their baseline clinical status, should antiepileptic therapy be initiated in the emergency department (ED) to prevent additional seizures?
- In patients with a first unprovoked seizure who have returned to their baseline clinical status in the ED, should the patient be admitted to the hospital to prevent adverse events?
- In patients with a known seizure disorder in which resuming their antiepileptic medication in the ED is deemed appropriate, does the route of administration impact recurrence of seizures?
- In ED patients with generalized convulsive status epilepticus who continue to have seizures despite receiving optimal dosing of a benzodiazepine, which agent or agents should be administered next to terminate seizures?

Target Population

Adult patients aged 18 years and older presenting to the emergency department (ED) with generalized convulsive seizures

Interventions and Practices Considered

1. Identification and treatment of precipitating medical conditions
2. Consideration of any patient brain injury or disease history
3. Hospitalization not required for first unprovoked seizure if patient has returned to clinical baseline in the emergency department (ED)
4. Intravenous (IV) or oral antiepileptic medication to prevent additional seizures
5. Pharmacologic agents (continued seizures following benzodiazepine)
    - Phenytoin
    - Fosphenytoin

- Valproate
- Levetiracetam
- Propofol
- Barbiturates

Major Outcomes Considered

- Seizure cessation
- Seizure recurrence
- Morbidity and mortality
- Achievement of therapeutic serum drug levels
- Adverse events
- Length of emergency department (ED) stay

Methodology

Methods Used to Collect/Select the Evidence

Hand-searches of Published Literature (Primary Sources)

Hand-searches of Published Literature (Secondary Sources)

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

The clinical policy was created after careful review and critical analysis of the medical literature. Searches of MEDLINE, MEDLINE InProcess, Cochrane Systematic Review Database, and Cochrane Database of Clinical Trials were performed. All searches were limited to English-language sources, human studies, and adults. All searches excluded pediatric or children, head trauma, brain mass or brain tumor, and immunocompromised immune system. Specific key words/phrases and years used in the searches are identified under each critical question in the original guideline document. In addition, relevant articles from the bibliographies of included studies and more recent articles identified by committee members and reviewers were included.

Number of Source Documents

Not stated

Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

Rating Scheme for the Strength of the Evidence

Strength of Evidence

Literature Classification Schema*

Design/Class	Therapy†	Diagnosis‡	Prognosis§
1	Randomized, controlled trial or meta-analysis of randomized trials	Prospective cohort using a criterion standard or meta-analysis of prospective studies	Population prospective cohort or meta-analysis of prospective studies

Design/Class	Therapy†	Diagnosis‡	Prognosis§
2	Nonrandomized trial	Retrospective observational	Retrospective cohort
			Case control
3	Case series Case report Other (e.g., consensus, review)	Case series Case report Other (e.g., consensus, review)	Case series Case report Other (e.g., consensus, review)

*Some designs (e.g., surveys) will not fit this schema and should be assessed individually.

†Objective is to measure therapeutic efficacy comparing interventions.

‡Objective is to determine the sensitivity and specificity of diagnostic tests.

§Objective is to predict outcome including mortality and morbidity.

Approach to Downgrading Strength of Evidence*

	Design/Class		
Downgrading	**1**	**2**	**3**
None	I	II	III
1 level	II	III	X
2 levels	III	X	X
Fatally flawed	X	X	X

*See the "Description of the Methods Used to Analyze the Evidence" field for more information.

Methods Used to Analyze the Evidence

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

All articles used in the formulation of this clinical policy were graded by at least 2 subcommittee members and assigned a Class of Evidence. In doing so, subcommittee members assigned design classes to each article, with design 1 representing the strongest study design and subsequent design classes (e.g., design 2, design 3) representing respectively weaker study designs for therapeutic, diagnostic, or prognostic clinical reports, or meta-analyses (see the "Rating Scheme for the Strength of the Evidence" field). Articles were then graded on dimensions related to the study's methodological features, including but not necessarily limited to randomization processes, blinding, allocation concealment, methods of data collection, outcome measures and their assessment, selection and misclassification biases, sample size, and generalizability. Using predetermined formulas related to the study's design, methodological quality, and applicability to the critical question, articles received a final Class of Evidence grade (i.e., Class I, Class II, Class III, or Class X) (Appendix B of the original guideline document). Articles identified with fatal flaws or that were not applicable to the critical question received a Class of Evidence grade "X" and were not used in formulating recommendations for this policy. Grading was done with respect to the specific critical questions; thus, the level of evidence for any one study may vary according to the question. As such, it was possible for a single article to receive different Classes of Evidence as different critical questions were answered from the same study. Question-specific Classes of Evidence grading may be found in the Evidentiary Table included at the end of the original guideline document.

Methods Used to Formulate the Recommendations

Expert Consensus

Description of Methods Used to Formulate the Recommendations

This policy is a product of the American College of Emergency Physicians (ACEP) clinical policy development process, including expert review, and is based on the existing literature; where literature was not available, consensus of emergency physicians was used.

When possible, clinically oriented statistics (e.g., likelihood ratios, number needed to treat [NNT]) were presented to help the reader better understand how the results may be applied to the individual patient. For a definition of these statistical concepts, see Appendix C in the original guideline document.

Rating Scheme for the Strength of the Recommendations

Strength of recommendations regarding each critical question were made by subcommittee members using results from strength of evidence grading, expert opinion, and consensus among subcommittee members according to the following guidelines:

Strength of Recommendations

Level A recommendations. Generally accepted principles for patient care that reflect a high degree of clinical certainty (i.e., based on evidence from 1 or more Class of Evidence I or multiple Class of Evidence II studies).

Level B recommendations. Recommendations for patient care that may identify a particular strategy or range of strategies that reflect moderate clinical certainty (i.e., based on evidence from 1 or more Class of Evidence II studies or strong consensus of Class of Evidence III studies).

Level C recommendations. Recommendations for patient care that are based on evidence from Class of Evidence III studies or, in the absence of any adequate published literature, based on expert consensus. In instances where consensus recommendations are made, "consensus" is placed in parentheses at the end of the recommendation.

There are certain circumstances in which the recommendations stemming from a body of evidence should not be rated as highly as the individual studies on which they are based. Factors such as heterogeneity of results, uncertainty about effect magnitude and consequences, and publication bias, among others, might lead to such a downgrading of recommendations.

Cost Analysis

A formal cost analysis was not performed and published cost analyses were not reviewed.

Method of Guideline Validation

External Peer Review

Internal Peer Review

Description of Method of Guideline Validation

Expert review comments were received from emergency physicians, neurologists, and individual members of the American Epilepsy Society, the American Academy of Neurology, the Epilepsy Foundation of America, the National Association of Epilepsy Centers, and the American College of Emergency Physician's (ACEP) Quality and Performance Committee. The draft was also open to comments from ACEP membership through *EM Today*. Their responses were used to further refine and enhance this policy; however, their responses do not imply endorsement of this clinical policy.

This clinical policy was approved by the ACEP Board of Directors, January 14, 2014.

This guideline was endorsed by the Emergency Nurses Association, March 5, 2014.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type of supporting evidence is identified and graded for each recommendation (see the "Major Recommendations" field).

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

Appropriate evaluation and management of adult patients presenting to the emergency department (ED) with seizures

Potential Harms

Table 2 and Table 3 in the original guideline document list adverse effects associated with the recommended pharmacologic agents.

Qualifying Statements

Qualifying Statements

- Policy statements and clinical policies are the official policies of the American College of Emergency Physicians (ACEP) and, as such, are not subject to the same peer review process as articles appearing in the journal. Policy statements and clinical policies of ACEP do not necessarily reflect the policies and beliefs of Annals of Emergency Medicine and its editors.
- This policy is not intended to be a complete manual on the evaluation and management of patients with seizures but rather a focused examination of critical issues that have particular relevance to the current practice of emergency medicine.
- It is the goal of the Clinical Policies Committee to provide an evidence-based recommendation when the medical literature provides enough quality information to answer a critical question. When the medical literature does not contain adequate empirical data to answer a critical question, the members of the Clinical Policies Committee believe that it is equally important to alert emergency physicians to this fact.
- Recommendations offered in this policy are not intended to represent the only diagnostic or management options available to the emergency physician. ACEP clearly recognizes the importance of the individual physician's judgment and patient preferences. Rather, this guideline defines for the physician those strategies for which medical literature exists to provide support for answers to the critical questions addressed in this policy.

Implementation of the Guideline

Description of Implementation Strategy

An implementation strategy was not provided.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Getting Better

Living with Illness

IOM Domain

Effectiveness

Timeliness

Identifying Information and Availability

Bibliographic Source(s)

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Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2004 May (revised 2014 Apr)

Guideline Developer(s)

American College of Emergency Physicians - Medical Specialty Society

Source(s) of Funding

American College of Emergency Physicians

Guideline Committee

American College of Emergency Physicians Clinical Policies Subcommittee (Writing Committee) on Seizures

Composition of Group That Authored the Guideline

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Financial Disclosures/Conflicts of Interest

Relevant industry relationships: Dr. Jagoda serves as the editor-in-chief of Emergency Medicine Practice, is a consultant and on the Advisory

Board for Pfizer and for Janssen Pharmaceuticals Inc, is on the Advisory Board for UCB Pharma, and is a consultant for AstraZeneca.

Relevant industry relationships are those relationships with companies associated with products or services that significantly impact the specific aspect of disease addressed in the critical questions.

Guideline Endorser(s)

Emergency Nurses Association - Professional Association

Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: Clinical policy: critical issues in the evaluation and management of adult patients presenting to the emergency department with seizures. Ann Emerg Med. 2004 May;43(5):605-25. [95 references]

Guideline Availability

Electronic copies: Available in Portable Document Format (PDF) from the American College of Emergency Physicians Web site .

Availability of Companion Documents

None available

Patient Resources

None available

NGC Status

This NGC summary was completed by ECRI on July 14, 2004. The information was verified by the guideline developer on August 13, 2004. This summary was updated by ECRI Institute on May 1, 2009 following the U.S. Food and Drug Administration advisory on antiepileptic drugs. This summary was updated by ECRI Institute on May 30, 2014. The updated information was verified by the guideline developer on June 5, 2014. This summary was updated by ECRI Institute on February 15, 2017 following the U.S. Food and Drug Administration advisory on general anesthetic and sedation drugs.

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